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K011400/S

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

According to the requirements of 21 CFR 807.92, the following information summarizes and provides sufficient detail to understand the basis for a determination of substantial equivalence. The information and data contained in this summary was obtained from studies performed by and for Denka Seiken Co. Ltd., where all data is also kept on file.

DEVICE NAME

Proprietary name: MRSA-Screen

Common name: A slide latex agglutination kit for the rapid detection of penicillin-binding protein PBP2' (2a), or PBP2' (PBP2a)

Classification name: Manual antimicrobial susceptibility test, Class 2

COMPARATIVE DEVICE

The Denka Seiken MRSA-Screen test was compared to three methods: the Oxacillin Screen Agar (Meuller Hinton Agar with 4% NaCl and Oxacillin (6 ug/mL) and MIC determination by microbroth dilution assay, both according to the NCCLS guidelines. The Oxacillin Agar Screen test was used as the predicate device to establish substantial equivalence. PCR *mecA* detection was also performed for genotyping purposes.

DEVICE DESCRIPTION

MRSA-Screen consists of latex reagent sensitized with a monoclonal antibody against penicillin-binding protein 2'(2a), or PBP2' (PBP2a), together with control latex and 2 extraction reagents to rapidly extract PBP2' from the bacterial cell membranes of MRSA. Extracts are prepared by boiling a suspension of *S. aureus* cells under alkaline conditions, followed by neutralization and a centrifugation step. The supernatant is subsequently mixed with the latex reagents on a test card and visible clumping or agglutination within three minutes with the sensitized latex but not the control latex confirms the presence of MRSA.

INTENDED USE

MRSA-Screen is a rapid and sensitive slide latex agglutination test for the detection of PBP2' (PBP2a) present in methicillin resistant *Staphylococci aureus* (MRSA) and is thus useful as an aid in identifying MRSA in clinical isolates of *S. aureus*.

Clinical significance

Strains of *S. aureus* with reduced susceptibility to pencillinase-resistant penicillins are categorrized as follows:

1) Methicillin-resistant *S. aureus* (MRSA), which produce the low-affinity penicillin binding protein PBP2', encoded by the *mec*A gene.

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2) borderline oxacillin-resistant *S. aureus* (BORSA), generally considered to be due to hyper-production of type A-lactamase by strains of phage group V, the 94-96 complex, that harbor the pBW15 plasmid.
3) strains with modified PBPs due to altered penicillin binding capacity as a result of point mutations or due to hyperproduction of PBPs (MODSA).

While the drug of choice for treating MRSA is vancomycin, the emergence of vancomycin-resistant enterococci and the discovery of strains of *S. aureus* with reduced susceptibility to vancomycin has made penicillin-resistant penicillins (PRP) the preferred treatment when strains are susceptible to these agents, especially since beta-lactam drugs are more easily absorbed in body fluids and tissues, cause fewer complications, do not select for vancomycin-resistant organsims and reduce costs in the treatment of hospitalized patients.

METHODOLOGY COMPARISON

All four methods are similar in that they are used to identify methicillin-resistant *Staphylococci aureus* in clinical isolates of *S. aureus* due to the *mecA* gene. The four methods differ in that

1) MRSA-Screen detects the presence of the penicillin binding protein 2' (PBP2') by a latex-enhanced antigen-antibody reaction with total time to results after primary culture of approximately 15 minutes.
2) MIC is a phenotypic test based on the ability of a strain of *S. aureus* to show resistance to oxacillin at various concentrations in broth microdilutions. The test requires 24 hours for results and also identifies methicillin resistance due to hyperproduction of beta-lactamase or modification of other penicillin-binding proteins.
3) Oxacillin agar screen is a phenotypic test based on the ability of a strain of *S. aureus* to show resistance to oxacillin when a given amount of bacterial cell growth is inoculated onto the agar plate. The test requires 24 hours for results and also identifies methcillin resistance due to hyperproduction of beta-lactamase or modification of other penicillin-binding proteins.
4) *mecA* PCR is a DNA-based amplification methodology to specifically detect the presence of the *mecA* gene encoding for the PBP2' protein in approximately 4 hours; although considered the gold standard, it is considered too complex for routine clinical use.

PERFORMANCE DATA

The MRSA-Screen test was evaluated and compared to the NCCLS reference method for the oxacillin agar screen test (predicate device) on 726 clinical isolates of coagulase-positive *S. aureus* collected at 3 geographically distibuted clinical laboratories* to challenge the test for a wide range of phenotypically and genotypically distinct isolates of *S. aureus* as well as on 201 fresh isolates of *S. aureus* at four geographically distributed clinical sites. In total, 927 isolates were tested and overall agreement between the two tests was 95.4%, summarized below:

*)Two hundred of the 726 "challenge strains" were clinical bloodstream isolates from an antimicrobial surveillance program and consited of 81 isolates from North America, 33 isolates from Latin America, 48 isolates from the Westerm Pacific and 38 isolates from Europe.

Type	MRSA-Screen	Oxacillin Screen	Agreement
MRSA	Positive	Growth	458/464 (98.7%)
MSSA	Negative	No growth	391/393 (99.5%)
BORSA	Negative	No growth	35/68 (51.4%)
MODSA	Negative	No growth	0/2 (0%)
		Total	884/927 (95.4%)

Note on discrepant results:
mecA analysis on 42 of the above discrepant strains revealed agreement of results between MRSA-Screen and PCR, and oxacillin agar screen and PCR, of 85.7% (36/42) and 14.3% (6/42), respectively.

Reproducibilty

Reproducibility of MRSA-Screen test results was determined as follows:

1) Using three lots of reagents, three operators and 1 strain of MRSA and 1 strain of MSSA with five replicates in a single run, the test gave the correct results each time. Furthermore, as part of stability studies this was repeated at 0, 3, 6, 9, 12 and 16 months with identical results.
2) Ten different well-characterized *S. aureus* strains (3 MRSA, 3 MSSA, 3 BORSA and 1 MODSA) were sent to three laboratories with each strain submitted five times in coded and blinded fashion. All 150 test results agreed with the expected results for 100% reproducibility: The three *mecA* positive strains were positive each time tested (45/45); the three MSSA and the three BORSA, negative (90/90); and the MODSA, which had an MIC of 16 ug/ml to oxacillin, similarily was negative in all tests (15/15) as expected.
3) 60 isolates (24 MSSA, 12 BORSA and 24 MRSA) at one of the three North American study sites mentioned above was retested by the MRSA-Screen test and correct results were obtained each time.
4) At a second of these three North American sites, a smaller subset (5 MRSA and 5 MSSA) were retested in triplicate and the MRSA-Screen test gave the correct result each time.
5) A total of 200 strains of *S. aureus* from a European study site were tested in duplicate with the results interpreted blindly by two different persons. All 120 MSSA and 80 MRSA tested gave the same correct results, except for one MSSA strain, which was read as a false positive by one person and correctly by the other.

   (Note: The 80 MRSA strains were carefully selected on the basis of molecular typing and having 60 different pulsed-field gel electrophoresis patterns PFGE as well as on the basis of showing various levels of resistance to oxacillin (35 heterogeneously and 45 homogeneously resistant isolates).

Conclusion of Performance Data and Clinical Benefits

MRSA-Screen is simple to perform, requires minimal training and provides highly accurate re-

sults more rapidly than traditional methods, which are not as reliable in detecting low-level oxacillin resistance nor in distinguishing borderline oxacillin resistant (BORSA) strains from true MRSA. Thus, it has the advantage over phenotypic methods in that it is not influenced by the various levels of expression of resistance, such as in highly heterogenously resistant isolates. Furthermore, it has the potential of being even more accurate than the detection of *mecA* as false positve results will not occur for strains that are *mecA* positive but unable to produce the PBP2' protein.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
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MAR 2 7 2002

Mr. Kevin Mangan
International Sales Department
Denka Seiken Co., Limited
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Chuo-Ku, Tokyo
Japan 103-0025

Re: k011400
Trade/Device Name: MRSA-Screen
Regulation Number: 21 CFR 866.1640
Regulation Name: Antimicrobial Susceptibility Test
Regulatory Class: Class II
Product Code: MYI
Dated: January 3, 2002
Received: January 3, 2002

Dear Mr. Mangan:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known): K011400

Device Name: MRSA-Screen

Indications For Use:

INTENDED USE

MRSA-Screen is a rapid and sensitive slide latex agglutination test for the detection of PBP (PBP2a) present in methicillin resistant *Staphylococci aureus* (MRSA) and is thus useful as a aid in identifying MRSA in clinical isolates of *S. aureus.*

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

(Division Sign-Off)
Division of [illegible]ratory Devices

510(k) Number K011400

Prescription Use ✓ OR Over-The-Counter Use ___
(Per 21 CFR 801.109)

(Optional Format 1-2-96)